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Short Communication

Epidemic Pleurodynia Caused by Coxsackievirus B3 at a Medical Center in Northern Taiwan

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Epidemic pleurodynia is seldom reported in Southeast Asia and there has been no report from Taiwan. We conducted a retrospective chart review of children ≤ 18 years of age in the National Taiwan University Hospital from January 1 to December 31, 2005. Epidemic pleurodynia was defined as an acute illness characterized by sharp localized pain over the chest or upper abdomen. Patients with known heart diseases or pulmonary consolidations were excluded. In total, 28 patients met the case definition of epidemic pleurodynia. Coxsackievirus B3 (CB3) was isolated in 15 (60%) of the 25 throat swab specimens. Four (14%) of the 28 patients presented chest wall tenderness and only one (6%) of the 18 patients tested had an elevated creatinine kinase level. Twenty-one (75%) of the 28 patients described pleuritic chest pains and 10 (45%) of the 22 chest radiographies exhibited pulmonary infiltrates or pleural effusions. Six patients were observed with tonsillar exudates and one was confirmed to have a CB3 urinary tract infection. The clinical features and radiological findings suggest that CB3-associated epidemic pleurodynia might be a disease of the pleura and occasionally spreads to nearby tissues, resulting in chest wall myositis, pulmonary infiltrates and myopericarditis.

KEYWORDS: chest pain, coxsackievirus B3, epidemic pleurodynia, exudative tonsillitis, pleuritis

Introduction

Epidemic pleurodynia is characterized by fever and sharp, spasmodic pain in the chest or upper abdomen. It was first described in 1872 by Daae and Homann during an outbreak of "acute rheumatism spread by contagion" in Norway,[1] and was best known as Bornholm disease after a similar outbreak on the island of Bornholm in Denmark.[2] The etiology of the disease was not established until 1949 when coxsackievirus B was identified as the causative agent.[3,4] Other agents subsequently implicated in outbreaks of pleurodynia included echovirus[5–9] and

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coxsackievirus A.[10,11] Classical textbook descriptions of this disease usually attribute the illness to a disorder of the muscle, but not the pleura or peritoneum.[1]

Reports of outbreaks of pleurodynia come primarily from Europe and North America. There are nearly no reports from Southeast Asia. In 2005, we noticed an increased number of pediatric patients diagnosed with epidemic pleurodynia. Clinical features of the patients involved did not conform to the common belief that epidemic pleurodynia was a muscle disorder. This report describes clinical features that may shed light on the pathophysiology of epidemic pleurodynia.

Methods

A retrospective chart review of patients aged ≤ 18 years at the Department of Pediatrics, National Taiwan University Hospital, was conducted from January 1 to December 31, 2005. Epidemic pleurodynia was defined as an acute illness characterized by sharp localized pain over the chest or upper abdomen, with or without fever (body temperature ≥ 38°C). Those with a history of underlying heart diseases and with radiological findings showing an obvious pneumonia with consolidation were excluded. For each case, the duration of fever and chest pain, and the presence of other associated symptoms were recorded.

Laboratory investigations included complete blood count with leukocyte differentials, creatinine kinase (CK) and its myocardial isoenzyme (CK-MB), troponin I, aspartate aminotransferase, electrocardiogram and chest radiography. Throat swabs, rectal swabs, stools and body fluid specimens were sent for virus isolation. Samples were inoculated into human embryonic fibroblasts (MRC-5), rhesus monkey kidney (LLC-MK2), laryngeal carcinoma (HEp-2) and human rhabdomyosarcoma cell cultures. When the enteroviral cytopathic effect involved more than 50% of the cell monolayer, the cells were scraped and an indirect immunofluorescence assay employing a monoclonal antibody (Chemicon International Inc., Temecula, CA, USA) was performed for enterovirus typing.

Results

Of the 28 patients with a clinical diagnosis of epidemic pleurodynia, 6 (21%) were hospitalized. Viral isolation was attempted from 25 children. Of the 16 (64%) children who tested positive for enterovirus; 15 were identified as coxsackievirus B3 (CB3), whereas the remaining one isolate could not be typed using indirect immunofluorescence assay. The isolation rate of specimens from different sites was 60% (15/25) for throat swabs, 33% (1/3) for rectal swabs, 100% (1/1) for stool samples and 100% (1/1) for urine.

The Table summarizes the clinical and laboratory characteristics of the 28 patients with epidemic pleurodynia. For the 28 patients, the median duration of chest pain was 4.5 days (range, 1–45 days), 21 (75%) described the pain as having "pleuritic" characteristics, defined as a sharp pain that may be aggravated during a deep breath and that may limit chest wall movement, and four (14%) presented chest wall tenderness. Other associated symptoms and signs observed included fever (median duration=3 days; range, 1–11 days), upper airway symptoms, gastrointestinal symptoms, headache, oral ulcers and skin rash (Table).

Blood tests were performed on 18 patients. Only one girl, aged 17 years, had an elevated serum CK value of 211 U/L (normal range, ≤ 167 U/L for females) and her chest radiography showed neither pulmonary infiltrates nor pleural effusions. Among the 22 patients that had chest radiographic examinations, localized or diffuse pulmonary infiltrates were observed in 10 (45%) patients (Figure) and pleural effusions were observed in three (14%) patients. Electrocardiograms were performed on 11 patients and were found to be abnormal in three (27%) patients, which included ST-T segment elevation at lead I–II and V2–6 ($n=1$), inverted T wave at lead V1–3 ($n=1$), and prolonged PR and QTc intervals ($n=1$).

Five (18%) of the 28 children experienced acute comorbid illness, including group A streptococcal tonsillitis, acute otitis media, myocarditis, orchitis and CB3-associated urinary tract infection. The patient with a clinical diagnosis of CB3 urinary tract infection was a boy aged 14 years who had proteinuria and microscopic hematuria (35–50 red blood cells observed per high power field). His urine culture yielded CB3 instead of bacteria.

Discussion

Although outbreaks of epidemic pleurodynia have been reported from different parts of the world since its first description in Scandinavia as Bornholm disease,[12,13] this is

Table. Characteristics for 28 pediatric patients with epidemic pleurodynia

Characteristics	*n* (%)
Age (yr)	
0–4	3 (11)
5–9	15 (53)
10–18	10 (36)
Sex	
Male	19 (68)
Female	9 (32)
Chronic comorbid illness	0 (0)
Symptoms and signs	
Fever	24 (86)
Chest pain with pleuritic characteristics[a]	21 (75)
Upper airway symptoms[b]	17 (61)
Gastrointestinal symptoms[c]	11 (39)
Headache	10 (36)
Tonsillar exudates	6 (21)
Chest wall tenderness	4 (14)
Oral ulcer	2 (7)
Skin rash	1 (4)
Abnormal leukocyte count[d] (*n*=18)	4 (22)
Abnormal CK value[e] (*n*=16)	1 (6)
Abnormal AST value[f] (*n*=11)	0 (0)
Abnormal electrocardiogram[g] (*n*=11)	3 (27)
Infiltrates or pleural effusions on chest radiography (*n*=22)	10 (45)

[a]Defined as sharp pain with breathing that may limit the chest wall movement; [b]include runny nose, cough, or sore throat; [c]include nausea, vomiting, or loose stools; [d]leukocyte count <4,000/μL (*n*=1) or >11,000/μL (*n*=3); [e]CK >190 U/L (males) or CK >167 U/L (females); [f]AST >40 U/L; [g]ST-T segment elevation at lead I–II and V2–6 (*n*=1), inverted T wave at lead V1–3 (*n*=1), and prolonged PR and QTc intervals (*n*=1). AST=aspartate aminotransferase; CK=creatinine kinase.

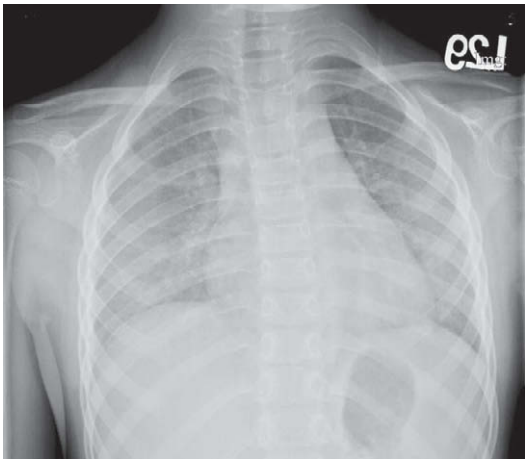

Figure. Posterior-anterior view of chest radiography showing bilateral interstitial infiltrates in a 6-year-old girl with right chest pain that could be aggravated by deep breathing. The thoracic vertebrae curved to the right side. The throat swab yielded the growth of coxsackievirus B3.

the first acknowledged incident in Taiwan. Asia, especially the southeastern region, has had fewer documented cases of epidemic pleurodynia.[13] It is likely that the disease might have escaped detection because some countries lack provisions for the appropriate virological tests. A correct and prompt recognition of the disease during endemic seasons curtails unnecessary usage of antibiotics and investigations.[14] In addition to the typical sudden onset of severe "stabbing" pain with pleuritic characteristics over the lower chest or upper abdomen after an incubation period of 2–5 days, minor constitutional symptoms have also been described. In our study, 36% of the patients described having headaches, 61% had upper airway symptoms, and 39% had gastrointestinal symptoms. The short course and rare occurrence of complications of epidemic pleurodynia helped to differentiate it from other less benign conditions.[14–16]

Epidemic pleurodynia is generally caused by coxsackievirus B, but less frequently results from echovirus serotypes 1, 6, 8, 9 and 19,[5–9] and from group A coxsackievirus serotypes 4, 6, 9 and 10.[10,11] Enteroviral isolation is more likely to be successful from feces during the acute phase of the illness.[13,17] A retrospective study of non-polio enteroviruses showed that stool cultures were positive for non-polio enteroviruses in 97% of clinical specimens, followed by throat swab cultures in 67% of clinical specimens.[17] The isolation rate of throat swab cultures in our study was 60%, which was comparable with reported viral isolation rates of 45–52% in previous outbreaks of epidemic pleurodynia.[3,7,13,14]

Since more than half of our patients were confirmed to have CB3 infection, it may be concluded that CB3 is responsible for this epidemic. Surveillance data from the Taiwan Centers for Disease Control also showed that from January 1 through to December 31, 2005, CB3 was the most common subtype, accounting for 28% of all

enterovirus isolates.[18] Coxsackievirus B is known to cause acute central nervous system infections, exanthems, acute respiratory diseases, myositis, myopericarditis and neonatal sepsis.[1] Clinical manifestations observed in this study, such as oral ulcers and exanthems, may also be seen in some other types of enterovirus infections. However, tonsillar exudates and urinary tract infections have been rarely described in enterovirus infections. To the best of our knowledge, this study may be the first to demonstrate the clear association between CB3 and both exudative tonsillitis and urinary tract infection.

Although many authors have reported that epidemic pleurodynia is a disease of the muscle instead of the pleura or peritoneum,[1,15,19] only one of the 18 patients tested in the present study had elevated serum aspartate aminotransferase or CK values. In addition, only a small proportion of our patients had chest wall tenderness, and none of them had other features that may characterize myositis of the chest wall, such as chest wall redness and swelling. More patients had chest films showing either localized or diffuse pulmonary infiltrates, as well as a small amount of pleural effusion. The majority of patients clearly stated that their chest pain could be aggravated by taking a deep breath, suggesting the presence of pleuritis. These findings suggest that CB3-induced epidemic pleurodynia is a disease mainly of the pleura. The inflammatory process may occasionally spread to nearby tissues, resulting in chest wall myositis, pulmonary infiltrates and myopericarditis.

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